

(FILE 'HOME' ENTERED AT 14:22:42 ON 18 JUN 1999)

FILE 'SCISEARCH, MEDLINE, CAPLUS, BIOSIS, CANCERLIT, AGRICOLA, GENBANK'  
ENTERED AT 14:22:50 ON 18 JUN 1999

L1 9926 S ECDYSONE  
L2 1144 S L1 AND RECEPTOR  
L3 2 S L2 AND (GENE TRANSFER)  
L4 106 S L2 AND MAMMAL?  
L5 73 S L4 AND EXPRESSION  
L6 20 S L5 AND INDUCIBLE  
L7 16 DUP REM L6 (4 DUPLICATES REMOVED)  
L8 16 SORT L7 PY  
L9 229 S L2 AND INDUCIBLE  
L10 23 S L9 AND MAMMAL?  
L11 19 DUP REM L10 (4 DUPLICATES REMOVED)  
L12 19 SORT L11 PY  
L13 25 S L1 AND (GENE THERAPY)  
L14 16 DUP REM L13 (9 DUPLICATES REMOVED)  
L15 25 SORT L13 PY  
L16 16 SORT L14 PY  
L17 0 S L2 AND VPECR  
E EVAN RONALD/AU  
L18 0 S E3  
E EVANS RONALD/AU  
L19 13 S E3  
L20 12 DUP REM L19 (1 DUPLICATE REMOVED)  
L21 12 SORT L20 PY

=> d 18 3.all

L8 ANSWER 3 OF 16 CAPLUS COPYRIGHT 1999 ACS  
AN 1994:209524 CAPLUS  
DN 120:209524  
TI Binding of members of the steroid/thyroid superfamily of receptors  
with the ultraspiracle receptor  
IN Evans, Ronald M.; McKeown Michael B.; Oro, Anthony E.; Segraves, William  
A.; Yao, Tso Pang  
PA Salk Institute for Biological Studies, USA  
SO PCT Int. Appl., 68 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM C12N015-12  
ICS C07K015-06  
CC 2-2 (Mammalian Hormones)  
Section cross-reference(s): 3, 12, 13  
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9401558	A2	19940120	WO 93-US6296	19930701
	WO 9401558	A3	19940526		
	W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9347697	A1	19940131	AU 93-47697	19930701
	JP 08501211	T2	19960213	JP 93-503431	19930701
	EP 804568	A2	19971105	EP 94-904904	19930701
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, PT, IE				
PRAI	US 92-907908		19920702		
	WO 93-US6296		19930701		
AB	Members of the steroid/thyroid superfamily of receptors can interact with the insect-derived ultraspiracle (usp) receptor, to form multimerics. The system is useful in achieving high-level expression of exogenous genes in transgenic systems using a steroid hormone-responsive system (no data). The interaction of a member of the steroid/thyroid superfamily of receptors with dimerization domain of the ultraspiracle receptor modulates the				

ability of the steroid/thyroid **receptor** to transactivate transcription of genes regulated by steroid or thyroid hormones in the presence of the cognate ligand for the **receptor**. The **usp receptor** was prep'd. by in vitro translation of the mRNA and shown to increase the binding of the retinoic acid **receptor** the .beta.RARE element. Mobility shift expts. demonstrated that the **usp receptor** formed heterodimers with the **mammalian nuclear receptors** TR.beta., VDR, and PPAR and affected their binding to the cognate regulatory element. A complex between **usp** and the **ecdysone receptor** had a very high affinity for DNA with the binding of the complex for DNA correlating with the functionality of the **ecdysone receptor** binding site on the target sequence.

- ST ultraspiracle steroid **receptor** heterodimer; thyroid **receptor** ultraspiracle heterodimer
- IT Genetic element  
RL: BIOL (Biological study)  
(PPAR-responsive element, **receptor** binding to, complex with ultraspiracle **receptor** for stimulation of)
- IT Gene  
RL: BIOL (Biological study)  
(exogenous, regulation of **expression** of, ultraspiracle **receptor** complexes with steroid/thyroid **receptor** for)
- IT Deoxyribonucleic acid sequences  
(of ultraspiracle gene of Drosophila melanogaster)
- IT Protein sequences  
(of ultraspiracle gene product of Drosophila melanogaster)
- IT Transcription, genetic  
(steroid/thyroid hormone **receptor**-dependent, stimulation of, formation of complex with ultraspiracle **receptor** in)
- IT Drosophila melanogaster  
(ultraspiracle gene product of, interaction with steroid/thyroid **receptors** of)
- IT Receptors  
RL: BIOL (Biological study)  
(ultraspiracle, complexes with steroid/thyroid **receptors**, formation of, increased DNA binding by, regulation of expression of exogenous genes by)
- IT Receptors  
RL: BIOL (Biological study)  
(PPAR (peroxisome proliferator-activated **receptor**), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)
- IT Receptors  
RL: BIOL (Biological study)  
(RAR-.alpha. (retinoic acid **receptor** .alpha.), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)
- IT Retinoids  
RL: BIOL (Biological study)  
(RAR-.alpha. **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)
- IT Receptors  
RL: BIOL (Biological study)  
(RAR-.beta. (retinoic acid **receptor** .beta.), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)
- IT Retinoids  
RL: BIOL (Biological study)  
(RAR-.beta. **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)
- IT Receptors  
RL: BIOL (Biological study)  
(RAR-.gamma. (retinoic acid **receptor** .gamma.), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)
- IT Retinoids  
RL: BIOL (Biological study)  
(RAR-.gamma. **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)
- IT Genetic element  
RL: BIOL (Biological study)  
(RARE (retinoic acid-responsive element), .beta.-, **receptor**

binding to, complex with ultraspiracle receptor for stimulation of)

IT Receptors  
RL: BIOL (Biological study)  
(TR (thyroid/steroid hormone receptor), ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Thyroid hormones  
(TR receptors, ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Steroids, biological studies  
RL: BIOL (Biological study)  
(TR receptors, ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Genetic element  
RL: BIOL (Biological study)  
(TRE (thyroid hormone-responsive element), receptor binding to, complex with ultraspiracle receptor for stimulation of)

IT Receptors  
RL: BIOL (Biological study)  
(ecdysteroid, ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Genetic element  
RL: BIOL (Biological study)  
(promoter, tissue-specific, expression of exogenous genes from, steroid-responsive element and steroid/thyroid and ultraspiracle receptors in)

IT Ecdysteroids  
(receptors, ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Genetic element  
RL: BIOL (Biological study)  
(steroid-responsive element, exogenous gene under control of, regulated expression of, ultraspiracle receptor complexes with steroid/thyroid receptor for)

IT Receptors  
RL: BIOL (Biological study)  
(thyroid hormone .alpha., ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Receptors  
RL: BIOL (Biological study)  
(thyroid hormone .beta., ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Gene, animal  
RL: BIOL (Biological study)  
(ultraspiracle, in expression of exogenous genes in steroid-inducible system)

IT Receptors  
RL: BIOL (Biological study)  
(vitamin D, ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Genetic element  
RL: BIOL (Biological study)  
(vitamin D-responsive element, receptor binding to, complex with ultraspiracle receptor for stimulation of)

IT Thyroid hormones  
RL: BIOL (Biological study)  
(.alpha. receptors, ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT Thyroid hormones  
RL: BIOL (Biological study)  
(.beta. receptors, ultraspiracle receptor complexes with, formation of, increased DNA binding by)

IT 138263-72-6, Protein (Drosophila melanogaster gene ultraspiracle reduced)  
RL: PRP (Properties)  
(amino acid sequence of, formation of complexes with steroid/thyroid receptor of, stimulation of gene expression by)

IT 154173-85-0  
RL: PRP (Properties)  
(amino acid sequence of, relationship to RXR receptors of)

IT 153679-02-8 153679-03-9 153679-04-0 153679-05-1  
RL: BIOL (Biological study)  
(ecdysone receptor binding to, stimulation by)

ultraspiracle receptor of)  
IT 138263-42-0  
RL: PRP (Properties  
(nucleotide sequence of)  
IT 153678-98-9 153678-99-0 153679-00-6 153679-01-7  
RL: BIOL (Biological study)  
(receptor binding to, stimulation by ultraspiracle  
receptor of)

L16 ANSWER 7 OF 16 CAPLUS COPYRIGHT 1999 ACS  
AN 1998:25131 CAPLUS  
DN 128:98563  
TI Modular assembly retroviral vectors for high level and ligand-modulatable gene expression  
IN Gage, Fred H.; Suhr, Steven T.  
PA Salk Institute for Biological Studies, USA; Gage, Fred H.; Suhr, Steven T.  
SO PCT Int. Appl., 54 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM A01N043-04  
ICS C12N005-00; C12N015-00; C12P021-00  
CC 3-2 (Biochemical Genetics)  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9748277	A1	19971224	WO 97-US8805	19970522
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
PRAI	AU 9732121	A1	19980107	AU 97-32121	19970522
	US 96-677025		19960620		
	WO 97-US8805		19970522		
AB	In accordance with the present invention, novel retroviral vectors contg. modified long terminal repeats (LTRs) which enable high level and ligand-modulatable expression of a desired gene product, even after prolonged periods of cellular quiescence, have been designed and constructed. Invention vectors overcome proviral transcriptional inactivation which occurs in cultured primary cells that are growth arrested due to environmental constraints such as contact inhibition and/or nutrient starvation. Invention vectors represent a class of retroviral vectors in which LTR-promoted proviral expression in infected cells may be maintained or increased, even in situations generally considered to be non-permissive for retroviral vectors. The family of retroviral vectors, collectively referred to as MARVs (for modular assembly retroviral vectors), are designed with LTR promoters that respond to specific constitutive or ligand-dependent transcription factors encoded by nucleic acids which have been introduced into the recombinant retroviral vectors. Three general elements combine to form MARV vectors: (1) native or mutated LTRs contg. regulatory elements responsive to a transactivator; (2) transactivator(s) optionally modified to provide a user-defined level of expression in the absence of ligand and higher-level expression in the presence of ligand; and (3) retroviral packaging signal. The first generation of MARV vectors were designed to respond to insect hormones (ecdysteroids) to stimulate transcription from the viral LTR. Examples of receptor complexes for ecdysteroids are composed of the Drosophila <i>ecdysone</i> receptor and the human retinoid X receptor or the Drosophila ultraspirelre receptor. A two-plasmid system is typically provided with antibiotic resistance markers, which enable the selection and characterization of infected cells <i>in vitro</i> . The co-functioning partner, referred to as MARSHA, is designed to encode a heterologous gene and a second antibiotic resistance gene.				
ST	retrovirus vector MARV MARSHA gene expression				
IT	Genetic elements				
	RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)				
	(HRE (hormone-responsive element); modular assembly retroviral vectors for high level and ligand-modulatable gene expression)				
IT	Plasmid vectors				
	Retroviral vectors				

(MARV and MARSHA; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Steroid receptors  
 Thyroid hormone receptors  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
     (TR (thyroid/steroid hormone receptor); modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Genetic elements  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
     (ecdysone-responsive element; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Transgenes  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (expression; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Hormone receptors  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
     (juvenile hormone, ultraspiracle; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Gene expression  
**Gene therapy**  
     (modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Ecdysteroid receptors  
**Ecdysteroids**  
 LTR (long terminal repeat)  
 Retinoid X receptor .alpha.  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
     (modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Genetic elements  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
     (packaging signal; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Antibiotic resistance  
     (selection vectors for; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT 60-54-8, Tetracycline 38778-30-2, Muristerone A 84371-65-3, RU486  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
     (modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

=> d 116 4 all

L16 ANSWER 4 OF 16 CAPLUS COPYRIGHT 1999 ACS  
 AN 1997:72295 CAPLUS  
 DN 126:85631  
 TI A gene switch comprising an insect **ecdysone** receptor or fusion product allows gene control by external chemical inducer and has agricultural and pharmaceutical applications  
 IN Jepson, Ian; Martinez, Alberto; Greenland, Andrew James  
 PA Zeneca Limited, UK; Jepson, Ian; Martinez, Alberto; Greenland, Andrew James  
 SO PCT Int. Appl., 121 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C12N015-12  
     ICS C12N015-85; C12N015-62; C07K014-72; C07K019-00; C12N005-10;  
         A61K038-16  
 CC 3-2 (Biochemical Genetics)  
     Section cross-reference(s): 1, 5, 10, 11, 12, 13  
 FAN.CNT 1  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 9637609	A1	19961128	WO 96-GB1195	19960520

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,  
 ES, FI, GE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,  
 LU, LV, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RU, SD, SE,  
 SG, SI  
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN  
 CA 2219121 AA 19961128 CA 96-2219121 19960520  
 AU 9657716 A1 19961211 AU 96-57716 19960520  
 EP 828829 A1 19980318 EP 96-914309 19960520  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 CN 1191568 A 19980826 CN 96-195739 19960520  
 JP 11506319 T2 19990608 JP 96-535473 19960520  
 NO 9705419 A 19980122 NO 97-5419 19971125  
 PRAI GB 95-10759 19950526  
 GB 95-13882 19950707  
 GB 95-17316 19950824  
 GB 96-5656 19960318  
 WO 96-GB1195 19960520

**AB** The invention relates to an insect steroid receptor protein which is capable of acting as a gene switch which is responsive to a chem. inducer enabling external control of the gene. The *Heliothis virescens ecdysone* receptor and the *Spodoptera exigua ecdysone* receptor or glucocorticoid receptor can be used. Expression of insect hormone receptors in plant, fungus, bacteria, or mammal can be useful. Plasmid constructs encoding insect hormone receptor fusion proteins with transactivator proteins of other sources are also included. Various promoters in plasmid constructs are included in further variations.

**ST** *ecdysone* receptor gene switch application; *Heliothis ecdysone* receptor gene switch application; transcription factor fusion *ecdysone* receptor application; *Spodoptera ecdysone* receptor gene switch application; insect *ecdysone* receptor gene switch application

**IT** Genetic elements  
 RL: AGR (Agricultural use); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (HRE (hormone-responsive element); gene switch comprising insect *ecdysone* receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

**IT** Plasmid vectors  
 (TEV-8; gene switch comprising insect *ecdysone* receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

**IT** Plasmid vectors  
 (TEV-B112; gene switch comprising insect *ecdysone* receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

**IT** Plasmid vectors  
 (TEVVP16-3; gene switch comprising insect *ecdysone* receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

**IT** GAL4 transcription factor  
 VP16 transcription factor  
 RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (fusion products; gene switch comprising insect *ecdysone* receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

**IT** RNA formation factors  
 RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (gene alcR, fusion products; gene switch comprising insect *ecdysone* receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

**IT** Animal cells  
 Bacteria (Eubacteria)  
 Corn  
 Fungi  
**Gene therapy**

Genetic engineering  
Heliothis virescens  
Insect (Insecta)  
Mammal (Mammalia)  
Plant (Embryophyta)  
Plasmid vectors  
Protein sequences  
Saccharomyces cerevisiae  
Spodoptera exigua  
Tobacco  
cDNA sequences  
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Ecdysteroids  
Glucocorticoids  
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Ecdysteroid receptors  
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Glucocorticoid receptors  
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Promoter (genetic element)  
RL: AGR (Agricultural use); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(p221.10GRE6; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(p221.9GRE6; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pJRIES1; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pJRIES2; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pJRIES3; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pJRIES4; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pMF6GREcRS; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pMF6GRHEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pMF6GRVP16HEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pMF6HG1PAT; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pMF7GREcRS; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pMF7GRHEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pMF7GRVP16HEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pSW GRE4; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors  
(pcDNA3GRHEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Gene regulation  
(switch; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT 185569-20-4P 185569-21-5P  
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT 185530-39-6 185530-40-9 185530-41-0 185569-19-1  
RL: AGR (Agricultural use); BPR (Biological process); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(nucleotide sequence; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

L8 ANSWER 5 OF 16 SCISEARCH COPYRIGHT 1999 ISI (R)  
TI ECDYSONE-INDUCIBLE GENE-**EXPRESSION** IN  
MAMMALIAN-CELLS AND TRANSGENIC MICE  
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF  
AMERICA, (16 APR 1996) Vol. 93, No. 8, pp. 3346-3351.  
ISSN: 0027-8424.  
AU NO D; YAO T P; EVANS R M (Reprint)  
AB During metamorphosis of *Drosophila melanogaster*, a cascade of morphological changes is triggered by the steroid hormone 20-OH **ecdysone** via the **ecdysone receptor**, a member of the nuclear **receptor** superfamily. In this report, we have transferred insect hormone responsiveness to **mammalian** cells by the stable **expression** of a modified **ecdysone receptor** that regulates an optimized **ecdysone** responsive promoter. Inductions reaching 4 orders of magnitude have been achieved upon treatment with hormone. Transgenic mice expressing the modified **ecdysone receptor** can activate an integrated **ecdysone** responsive promoter upon administration of hormone. A comparison of tetracycline-based and **ecdysone**-based **inducible** systems reveals the **ecdysone** regulatory system exhibits lower basal activity and higher inducibility. Since **ecdysone** administration has no apparent effect on **mammals**, its use for regulating genes should be excellent for transient **inducible expression** of any gene in transgenic mice and for gene therapy.



L8 ANSWER 3 OF 16 CAPLUS COPYRIGHT 1999 ACS  
TI Binding of members of the steroid/thyroid superfamily of **receptors**  
with the ultraspiracle **receptor**  
SO PCT Int. Appl., 68 pp.  
CODEN: PIXXD2  
IN Evans, Ronald M.; McKeown Michael B.; Oro, Anthony E.; Segraves, William  
A.; Yao, Tso Pang  
AB Members of the steroid/thyroid superfamily of **receptors** can  
interact with the insect-derived ultraspiracle (usp) **receptor**,  
to form multimerics. The system is useful in achieving high-level  
**expression** of exogenous genes in transgenic systems using a  
steroid hormone-responsive system (no data). The interaction of a member  
of the steroid/thyroid superfamily of **receptors** with  
dimerization domain of the ultraspiracle **receptor** modulates the  
ability of the steroid/thyroid **receptor** to transactivate  
transcription of genes regulated by steroid or thyroid hormones in the  
presence of the cognate ligand for the **receptor**. The usp  
**receptor** was prep'd. by in vitro translation of the mRNA and shown  
to increase the binding of the retinoic acid **receptor** the  
.beta.RARE element. Mobility shift expts. demonstrated that the usp  
**receptor** formed heterodimers with the **mammalian nuclear**  
**receptors** TR.beta., VDR, and PPAR and affected their binding to  
the cognate regulatory element. A complex between usp and the  
**ecdysone receptor** had a very high affinity for DNA with  
the binding of the complex for DNA correlating with the functionality of  
the **ecdysone receptor** binding site on the target

L8 ANSWER 1 OF 16 SCISEARCH COPYRIGHT 1999 ISI (R)

TI ECDYSTEROID-DEPENDENT REGULATION OF GENES IN **MAMMALIAN**-CELLS BY  
A DROSOPHILA **ECDYSONE RECEPTOR** AND CHIMERIC  
TRANSACTIVATORS

SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF  
AMERICA, (15 JUL 1992) Vol. 89, No. 14, pp. 6314-6318.  
ISSN: 0027-8424.

AU CHRISTOPHERSON K S; MARK M R; BAJAJ V; GODOWSKI P J (Reprint)

AB Steroid **receptors** are members of a large family of transcription factors whose activity is tightly regulated by the binding of their cognate steroid ligand. **Mammalian** steroid hormone **receptors** have been exploited to obtain the regulated **expression** of heterologous genes in **mammalian** cells. However, the utility of these systems in cultured cells and transgenic animals is limited by the presence of endogenous steroids and their **receptors**. We show that a Drosophila **ecdysone receptor** can function in cultured **mammalian** cells as an ecdysteroid-dependent transcription factor. The activity of the **ecdysone receptor** was not induced by any of the **mammalian** steroid hormones tested. The DNA-binding and transactivation activities of viral, **mammalian**, or bacterial proteins were rendered ecdysteroid-dependent when fused to the ligand-binding domain of the **ecdysone receptor**. The **ecdysone receptor** may prove useful in selectively regulating the **expression** of endogenous or heterologous genes in

L8 ANSWER 10 OF 16 MEDLINE  
TI Mammalian expression of transmembrane  
receptors for pharmaceutical applications.  
SO BIOCHEMICAL SOCIETY TRANSACTIONS, (1998 Nov) 26 (4) 699-704. Ref: 26  
Journal code: E48. ISSN: 0300-5127.  
AU Rhodes A D; Bevan N; Patel K; Lee M; Rees S  
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expressing recombinant receptors have been described. Each is  
suited to a different aspect of the study of receptors and their  
behaviour. IRES-based vectors are ideal for creating stable  
mammalian cell lines suitable for screening receptors  
using a signalling readout. Unlike traditional vectors they result in  
almost 100% of cell lines generated expressing a particular  
receptor, thus increasing the efficiency of cell line generation  
and increasing the chance of higher expression-level cell lines  
being generated. They may also be utilized to express more than one  
protein of interest, for example it is possible to co-express a particular  
receptor with a particular signalling protein or trafficking  
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expression system is ideal for studying receptor  
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expression levels in an identical cellular background thus making  
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activity in the absence of agonist. The SFV expression system is  
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mammalian cell. It is thus a good system for purifying  
receptors for structural analysis and for providing material for  
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12 ANSWER 14 OF 19 BIOSIS COPYRIGHT 1999 BIOSIS  
TI Generation of transgenic mice with expression of the **ecdysone**  
**inducible** system in the central nervous system.  
SO Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 71.  
Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part 1  
Los Angeles, California, USA November 7-12, 1998 Society for Neuroscience  
. ISSN: 0190-5295.  
AU Kostich, W. A. (1); Neal, R. G.; Dinchuk, J. E.; Focht, R. J.; Margolis,  
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L16 ANSWER 7 OF 16 CAPLUS COPYRIGHT 1999 ACS  
TI Modular assembly retroviral vectors for high level and ligand-modulatable gene expression  
SO PCT Int. Appl., 54 pp.  
CODEN: PIXXD2  
IN Gage, Fred H.; Suhr, Steven T.  
AB In accordance with the present invention, novel retroviral vectors contg. modified long terminal repeats (LTRs) which enable high level and ligand-modulatable expression of a desired gene product, even after prolonged periods of cellular quiescence, have been designed and constructed. Invention vectors overcome proviral transcriptional inactivation which occurs in cultured primary cells that are growth arrested due to environmental constraints such as contact inhibition and/or nutrient starvation. Invention vectors represent a class of retroviral vectors in which LTR-promoted proviral expression in infected cells may be maintained or increased, even in situations generally considered to be non-permissive for retroviral vectors. The family of retroviral vectors, collectively referred to as MARVs (for modular assembly retroviral vectors), are designed with LTR promoters that respond to specific constitutive or ligand-dependent transcription factors encoded by nucleic acids which have been introduced into the recombinant retroviral vectors. Three general elements combine to form MARV vectors: (1) native or mutated LTRs contg. regulatory elements responsive to a transactivator; (2) transactivator(s) optionally modified to provide a user-defined level of expression in the absence of ligand and higher-level expression in the presence of ligand; and (3) retroviral packaging signal. The first generation of MARV vectors were designed to respond to insect hormones (ecdysteroids) to stimulate transcription from the viral LTR. Examples of receptor complexes for ecdysteroids are composed of the Drosophila **ecdysone** receptor and the human retinoid X receptor or the Drosophila ultraspireacle receptor. A two-plasmid system is typically provided with antibiotic resistance markers, which enable the selection and characterization of infected cells in vitro. The co-functioning partner, referred to as MARSHA, is designed to encode a heterologous

L16 ANSWER 4 OF 16 CAPLUS COPYRIGHT 1999 ACS

TI A gene switch comprising an insect **ecdysone** receptor or fusion product allows gene control by external chemical inducer and has agricultural and pharmaceutical applications

SO PCT Int. Appl., 121 pp.

CODEN: PIXXD2

IN Jepson, Ian; Martinez, Alberto; Greenland, Andrew James

AB The invention relates to an insect steroid receptor protein which is capable of acting as a gene switch which is responsive to a chem. inducer enabling external control of the gene. The *Heliothis virescens* **ecdysone** receptor and the *Spodoptera exigua* **ecdysone** receptor or glucocorticoid receptor can be used. Expression of insect hormone receptors in plant, fungus, bacteria, or mammal can be useful. Plasmid constructs encoding insect hormone receptor fusion proteins with transactivator proteins of other sources are also included. Various promoters in